

## **REMARKS**

The present communication responds to the Office Action dated July 1, 2008. In that Office Action, the Examiner withdrew the previously indicated allowability of claim 4 and rejected claims 1, 2, 6, 9-11 and 13-23 under 35 U.S.C. § 103(a). Reconsideration and allowance are respectfully requested at least for the reasons discussed below.

### **Rejections under 35 U.S.C. § 103(a)**

#### *Rejection over the '432 Patent in view of the '104 Patent*

Claims 1, 2, 6, 9-11 and 13-18 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Wolfinbarger, Jr. et al. (US 5,977,432) (“the ‘432 Patent”) in view of Wolfinbarger, Jr. (US 5,976,104) (“the ‘104 Patent”). This rejection is traversed at least for the following reasons.

The Examiner previously indicated allowability of claim 4 and, thus, the limitations of claim 4 were written into claim 1. In the current rejection the Examiner explains, “The indicated allowability of claim 4 is withdrawn in view of a new interpretation of Wolfinbarger, Jr. et. al. (US 5,977,432).” It is thus noted that the allowance was not withdrawn in light of new art found by the Examiner but because the Examiner has somehow altered his interpretation of art that has twice previously been cited in this case (Office Action dated May 15, 2007 and Office Action dated January 10, 2008). With the withdrawal of allowability, claim 1 has been amended to remove the limitation of previously cancelled claim 4 and that limitation has been written into new claim 47.

Claim 1 recites, among other things, “centrifuging the tissue in a centrifuge with a flowing pathogen solvent reducing solution wherein the solution is flowed continuously to and away from the centrifuge” with “the centrifuging causing penetration of the pathogen reducing solution into substantially all of the cavities of the tissue”.

The Examiner is combining the teachings from the ‘432 Patent regarding centrifugation with the teachings from the ‘104 Patent regarding fluids. The ‘432 Patent and the ‘104 Patent were filed by the same inventor, and assigned to the same assignee, within approximately 1 year.

Accordingly, the inventor of the ‘432 Patent (the later-filed patent) was aware of the teachings of the ‘104 Patent at the time of filing the ‘432 Patent. Indeed, the inventor incorporated the ‘104 Patent into the specification of the ‘432 Patent in its entirety and yet, as discussed below, chose to specifically teach away from items in the ‘104 Patent such as continuous flow.

To develop an obviousness rejection of claim 1, the Examiner modifies the teachings of the ‘432 Patent with teachings from the ‘104 Patent. The Examiner concedes that the ‘432 Patent “is silent with respect to continuously flowing the solvent solution to and away from the centrifuge during the centrifuging.” *Current Office Action, page 3*. The Examiner then asserts that the ‘104 Patent teaches “another method of bone treatment wherein the solvent solution is flowed continuously to and away (sic) the treatment chamber, permitting complete removal of the bone marrow and continuous monitoring of bone marrow removal from the graft.” *Current Office Action, page 3*.

The Applicants respectfully submit that the combination of the ‘432 Patent and the ‘104 Patent is improper because there is no motivation to combine the references and because the ‘104 Patent explicitly teaches away from such combination.

The ‘432 Patent discloses a multi-step batch process for removal of bone marrow from the interstitial lumen and cancellous bone space through creation of a centrifugational force. *The ‘432 Patent, col. 4, ll. 21-25*. The process begins with a series of pre-clean or incubation procedures, including one or more of lavaging, soaking, sonicating, and agitating the cut bone grafts in cleaning solutions. *The ‘432 Patent, col. 7, ll. 52 – 61*. The bone graft is then transferred in a hydrogen peroxide solution to a centrifuge tube and centrifuged for a specified period. *The ‘432 Patent, col. 12, ll. 20-22*. Subsequently, the bone grafts are removed from their centrifuge tubes and again incubated and/or cleaned by one or more of lavaging, soaking, sonicating, and agitating the cut bone grafts in cleaning solutions. *The ‘432 Patent, col. 7, ll. 52 – 61*. The bone grafts are then subjected to a series of washing solutions before experiencing a centrifuging process, sonication, and further soaking. *The ‘432 Patent, col. 12, ll. 34-62*. In sum, the ‘432 Patent discloses a series of batch cleaning/incubating/washing procedures wherein a substantial portion involves the treatment of a bone graft outside of a centrifuge.

The ‘104 Patent does not remedy the disclosure deficiencies of the ‘432 Patent at least because the combination is improper. The Examiner is respectfully reminded that “rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *In re Kahn*, 441 F.3d 977 (CA Fed. 1996) (cited with approval in *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727 (2007)). While the Examiner has articulated some reasoning for combining the ‘432 Patent and the ‘104 Patent, the Applicants respectfully submit that the articulated reasoning of the Examiner ignores the teachings of the ‘432 Patent and the ‘104 Patent.

In his articulated rationale for modifying the ‘432 Patent with the teachings of the ‘104 Patent, the Examiner asserts:

It would have been obvious to one of ordinary skill in the art at the time of the invention to provide a means to continuously introduce to and remove solvent from the centrifuge of [the ‘432 Patent], in order to continually monitor removal of bone marrow from the graft of [the ‘432 Patent] and effectively remove bone marrow from the graft.

The Examiner then refers to Col. 3, ll. 5-8 of the ‘432 Patent to support his statement. That portion of the ‘432 Patent states:

The presently claimed process differs from prior art processes, including those disclosed in U.S. Pat. Nos. 5,333,626 and 5,513,662, in that the present process uses centrifugal force to remove bone marrow elements from the bone graft.

While that portion of the ‘432 Patent notes the use of centrifugal force to remove bone marrow, it is only to contrast it with the prior art. The ‘432 Patent, taken as a whole, discusses a multi-step process by which bone marrow is removed including, as described above, several pre-cleaning steps, centrifugation, and sonication. *The ‘432 Patent, col. 11, l. 62 – col. 12, l. 62*. Given the multiple different steps used to effect bone marrow removal, including multiple different types of apparatus (basins, centrifuges, and others) with multiple different types of solutions, it is unlikely that one skilled in the art would be compelled to continually monitor removal of bone marrow specifically during centrifugation. Indeed, the ‘432 Patent specifically discusses monitoring removal of the bone marrow. As disclosed in the ‘432 Patent, monitoring may include taking

core samples of bone plugs, solubilizing bone marrow from a bone plug sample, visual inspection using an electron microscope, as well as visual inspection with the naked eye. *The '432 Patent, col. 11, ll. 1-9.* Furthermore, much, if not all of the “monitoring” of the ‘432 Patent occurs outside of the centrifuge. *The '432 Patent, col. 11, ll. 9-60.* The Applicants thus respectfully submit that continual monitoring of a subset of the multi-step process using a means that is specifically taught against (discussed below) would not be obvious to one skilled in the art at the time the invention was made.

Beyond the lack of rational or suggestion for making the ‘432 Patent and the ‘104 Patent combination, the combination of the ‘432 Patent and the ‘104 Patent further is improper at least because the ‘432 Patent explicitly teaches away from the use of solution flow, continuous or otherwise, during its process:

The use of more traditional flushing procedures to remove bone marrow involves the use of pressurized flow of solution as a rapidly moving stream which dislodges bone marrow by impact of the solvent on the bone graft. Such procedures tend to generate aerosols of tissue and solvent which can be hazardous to processing personnel. The present invention virtually eliminates this hazard. *The '432 Patent, col. 8, ll. 23-29.*

The Examiner is respectfully directed to *Gillette Co. v. S.C. Johnson & Sons, Inc.*, 16 USPQ2d 1923 (Fed. Cir. 1990) where the Federal Circuit held that prior art which would “discourage” the ordinarily skilled artisan from attempting the claimed invention cannot validly support a rejection under 35 U.S.C. § 103. By disparaging the use of flowing solution in the art, the ‘432 Patent has unequivocally discouraged the skilled artisan from employing a flow of solution. Accordingly, a rejection under § 103 which attempts to combine the ‘432 Patent with any reference for the purpose of teaching flow of solution is clearly improper.

As still further support of nonobviousness, Applicants note that the ‘104 Patent is incorporated in its entirety into the ‘432 Patent specification. *The '432 Patent, col. 2, l. 64 – col. 3, l. 2.* In other words, the ‘432 Patent disclosed the recirculation method of the ‘104 Patent and failed not only to disclose the combination, but also failed to teach or suggest that a recirculation method may be employed in its process. Rather, the ‘432

Patent elected to explicitly teach away from the use of solution flow, continuous or otherwise, and to exclusively disclose and emphasize a batch cleaning process, much of it occurring outside of a centrifuge. Such an emphasis, especially in light of incorporation of the '104 Patent, strongly teaches away from the continuous solution flow cleaning of a tissue in a centrifuge such as recited in ““wherein [pathogen solvent reducing] solution is flowed continuously to and away from the centrifuge containing the tissue during centrifuging” of claim 1.

In summary, the Applicants respectfully submit that the combination of the '432 Patent and the '104 Patent is improper. First, the Applicants respectfully submit that there is no reasonable rationale to combine the teachings of the '432 Patent and the '104 Patent, as advanced by the Examiner, except from using Applicants' invention as a template through hindsight reconstruction of Applicant's claims. Such hindsight reconstruction is impermissible. Second, even using hindsight, such combination is improper and would not be done because the '432 Patent explicitly teaches away from the teachings of the '104 Patent that the Examiner attempts to combine with the '432 Patent. Third, the combination does not result in the claimed invention at least because, arguably, the teachings are already combined to the extent the inventors considered proper by incorporation by reference of the '104 Patent into the '432 Patent specification. The Applicants thus respectfully submit that claim 1, and all claims depending therefrom, is in condition for allowance. Reconsideration and withdrawal of the rejection are thus respectfully requested.

*Rejection over the '432 Patent in view of the '104 Patent and further in view of Morris et al.*

Claims 19, 22, and 23 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Wolfinbarger, Jr. et al. (US 5,977,432) in view of Wolfinbarger, Jr. (US 5,976,104) as applied to claim 17 above, and further in view of Morris et al. (WO 01/58497). This rejection is traversed at least for the reasons discussed below.

Each of claims 18, 22, and 23 depend from claim 1. Claim 1 recites, among other things, “centrifuging the tissue in a centrifuge with a flowing pathogen solvent reducing solution wherein the solution is flowed continuously to and away from the centrifuge”. As discussed above, the combination of the '432 Patent and the '104 Patent is improper and does not make

obvious claim 1. Not only does the ‘432 Patent not disclose the use of solution flow during its process, as previously noted, the ‘432 Patent explicitly teaches away from the use of solution flow, continuous or otherwise, during its process.

Morris does not remedy the deficiencies of the combination of the ‘432 Patent and the ‘104 Patent. Rather, Morris teaches an apparatus for treating the interior of a fluid permeable workpiece by establishing a pulsatile flow of fluid using pressure differentials. More specifically, in the method of Morris, an end of a bone is placed in a first chamber and another end of the bone is placed in a second chamber. *Morris, page 12*. Alternating pressure cycles between the first chamber and second chamber is then provided to achieve a pulsatile type flow through the bone. *Morris, page 12*. Morris does not disclose, teach, or suggest continuously flowing a liquid. Accordingly, Morris does not disclose, teach, or suggest wherein a liquid is flowed continuously to and away from a centrifuge containing tissue during centrifuging.

Thus, none of the ‘432 Patent, the ‘104 Patent, or Morris, alone or in combination, disclose, teach, or suggest, at least, “centrifuging the tissue in a centrifuge with a flowing pathogen solvent reducing solution wherein the solution is flowed continuously to and away from the centrifuge,” as recited by claim 1. The Applicants respectfully submit that claims 18, 22, and 23 are allowable at least for the reasons discussed with respect to claim 1. Reconsideration and withdrawal of the rejection are thus respectfully requested.

*Rejection over the ‘432 Patent in view of the ‘104 Patent and further in view of the ‘970 Patent*

Claims 20 and 21 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Wolfinbarger, Jr. et al. (US 5,977,432) in view of Wolfinbarger, Jr. (US 5,976,104) as applied to claim 17 above, and further in view of Wolfinbarger, Jr., et al. (US 6,293,970). This rejection is traversed at least for the following reasons.

Each of claims 20 and 21 depend from claim 1. Claim 1 recites, among other things, “centrifuging the tissue in a centrifuge with a flowing pathogen solvent reducing solution wherein the solution is flowed continuously to and away from the centrifuge”. As discussed above, the combination of the ‘432 Patent and the ‘104 Patent is improper and does not make obvious claim 1. Not only does the ‘432 Patent not disclose the use of solution flow during its

process, as previously noted, the ‘432 Patent explicitly teaches away from the use of solution flow, continuous or otherwise, during its process.

The ‘970 Patent does not remedy the deficiencies of the combination of the ‘432 Patent and the ‘104 Patent. The ‘970 Patent teaches a plasticized dehydrated or freeze-dried bone and/or soft tissue product. *The ‘970 Patent, Abstract.* The Examiner cites the ‘970 Patent for disclosing a process of sterilizing a bone graft followed by infusion with a plasticizer and that the plasticizer may be effect in improving graft brittleness. Even were the ‘970 Patent to teach what the Examiner suggests, the ‘970 Patent does not disclose, teach, or suggest “centrifuging the tissue in a centrifuge with a flowing pathogen solvent reducing solution wherein the solution is flowed continuously to and away from the centrifuge,” as recited by claim 1.

Thus, none of the ‘432 Patent, the ‘104 Patent, or the ‘970 Patent, alone or in combination, disclose, teach, or suggest “centrifuging the tissue in a centrifuge with a flowing pathogen solvent reducing solution wherein the solution is flowed continuously to and away from the centrifuge,” as recited by claim 1. The Applicants respectfully submit that claims 20 and 21 are allowable at least for the reasons discussed with respect to claim 1. Reconsideration and withdrawal of the rejection are thus respectfully requested.

**Conclusion**

This application now stands in allowable form and reconsideration and allowance is respectfully requested.

This response is being submitted on or before November 1, 2008, with the required fee for a 1-month extension of time, making this a timely response. It is believed that no additional fees are due in connection with this filing. However, the Commissioner is authorized to charge any additional fees, including extension fees or other relief which may be required, or credit any overpayment and notify us of same, to Deposit Account No. 04-1420.

Respectfully submitted,

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